



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
|-----------------|-------------|----------------------|---------------------|------------------|

09/684,061

10/06/2000

Stephen H. Bartelmez

0450-0031.30

2847

7590

05/15/2002

Iota Pi Law Group
P O Box 60850
Palo Alto, CA 94306-0850

EXAMINER

ZARA, JANE J

ART UNIT

PAPER NUMBER

1635

DATE MAILED: 05/15/2002

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/684,061

Applicant(s)

BARTELMEZ ET AL.

Examiner

Jane Zara

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 February 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-18 and 20 is/are rejected.
- 7) ☒ Claim(s) 19 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 11.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

File

Application/Control Number: 09/684,061

Page 2

Art Unit: 1635

DETAILED ACTION

5/11/14
This Office action is in response to the communication filed February 18¹⁹, 2002, Paper No. 10.

Claims 1-20 are pending in the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments and Amendments

Withdrawn Rejections

Rejection of claims 4, 8, 13 and 18-20 under 35 U.S.C. 112, second paragraph, is withdrawn in light of Applicants' arguments and amendments filed February 18, 2002, Paper No. 10.

Rejection of claims 17 and 19 under 35 U.S.C. 102(b), as being anticipated by Mitani et al, is withdrawn in light of Applicants' arguments and amendments filed February 18, 2002, Paper No. 10.

Rejection of claim 19 under 35 U.S.C. 103(a) as being unpatentable over Mitani et al in view of Baracchini et al is withdrawn in light of Applicants' arguments filed February 18, 2002, Paper No. 10.

Art Unit:1635

Maintained Rejections

Claims 5 and 14 are rejected under 35 U.S.C. 112, second paragraph, for the reasons of record set forth in the Office action mailed July 31, 2001, Paper No. 8.

The structures referred to in the claims can be claimed by name, and need not refer to figure numbers.

Claims 1-16 and 20 are rejected under 35 U.S.C. 112, first paragraph, for lacking enablement over the broad scope claimed for the reasons of record set forth in the Office action mailed July 31, 2001, Paper No. 8.

Applicant's arguments filed February 18, 2002, have been fully considered but they are not persuasive. Applicants argue that the claimed invention is enabled because it does not require undue experimentation to modulate hematopoietic stem cell differentiation comprising the administration of antisense oligomers directed to an mRNA preferentially expressed in stem cells. It is further argued that enablement exists for the broad scope claimed because sufficient examples have been provided in the instant disclosure (i.e. example 2 provides data for decreased number of high proliferative potential colony forming cells (HPP-CFC) following in vitro administration of an antisense oligonucleotide which targets the zinc finger protein EVI-1). Contrary to Applicants' assertions, the examples provided in the instant disclosure, comprising an observed decrease in HPP-CFC following the in vitro administration of antisense oligonucleotide of SEQ ID NO: 1, which specifically targets and inhibits the expression of EVI-1, does not enable the broad scope of the claimed invention, comprising a method of modulating

Art Unit:1635

hematopoietic stem cell differentiation in vitro and in vivo comprising the administration of any antisense which targets any mRNA that is preferentially expressed in any stem cell, and which administration comprises in vitro, in vivo or ex vivo administration. The in vitro administration of SEQ ID NO: 1 to LTR-HSC enriched stem cells is not enabling for or representative of the ability to successfully administer any and/or all antisense and target any and/or all stem cells in vitro, in vivo and/or ex vivo harboring any and/or all mRNA which (are) preferentially expressed in any stem cells, and further whereby the expression of such a broad array of target genes is successfully and appropriately inhibited and hematopoietic stem cell differentiation is modulated. In vitro results are not enabling for in vivo or ex vivo target cell delivery and target mRNA inhibition. In vivo and ex vivo efficacy using antisense is highly unpredictable, and further experimentation is required to enable such broad scope, whereby hematopoietic stem cell differentiation is successfully modulated in an organism comprising the administration of any antisense which targets any mRNA which is preferentially expressed in any stem cell.

Claims 17, 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mitani et al in view of Baracchini et al, for the reasons of record set forth in the Office action mailed July 31, 2001, Paper No. 8.

Applicant's arguments filed February 18, 2002, have been fully considered but they are not persuasive. Applicants argue that the obviousness rejection of record is improper because it involved hindsight construction to combine the teachings of Mitani and Baracchini because numerous oligonucleotide modifications are taught by Baracchini and furthermore that Mitani is

Art Unit:1635

silent regarding oligonucleotide modifications, and, according to Applicants' assertions, there is no logical reason for combining the references or Mitani and Baracchini. Contrary to Applicants' assertions, the means and motivation for inhibiting EVI-1 - a gene preferentially expressed in hematopoietic stem cells - using antisense were provided by Mitani. Mitani teaches inhibition of EVI-1 DNA binding domain expression in vitro using antisense which target EVI-1 mRNA, and Mitani teaches a correlation between EVI-1 DNA binding domain expression and anchorage independent growth of leukemic cells, and the role of EVI-1 in myeloblast transformation (differentiation). Baracchini teaches the advantages of incorporating backbone modifications such as PNAs and methyl phosphonates (i.e. substantially uncharged backbones) into antisense oligonucleotides for enhancing desired properties such as antisense stability and target binding (See Baracchini at col. 6, lines 18-57, for a description of such "preferred embodiments"). One of ordinary skill in the art would have been motivated to incorporate such modifications into antisense oligonucleotides because it was known that such modifications enhance target binding and stability of antisense oligonucleotides. One of ordinary skill in the art would have been motivated to optimize target cell uptake by active or facilitated transport using design choices for oligonucleotides which were known in the art (See especially col 6, lines 27-34 and col 7, lines 39-67 of Baracchini). One of ordinary skill would have been motivated to inhibit the expression of EVI-1 DNA binding domain expression in blood stem cells because a correlation between preferentially expressed EVI-1 and neoplastic transformation had been taught previously by Mitani. One of ordinary skill in the art would have expected that a target gene's expression

Art Unit:1635

would be inhibited in vitro comprising antisense which specifically target the initiation region of a target gene (See especially col. 9, lines 19-42 of Baracchini). Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Allowable Subject Matter

Claim 19 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however,

Art Unit:1635

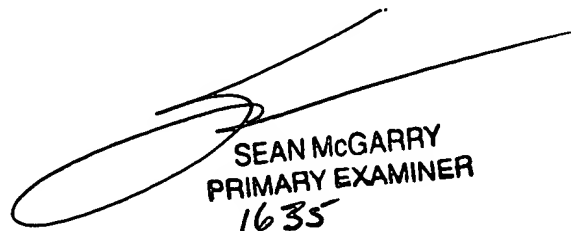
will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is (703) 306-5820. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JZ

May 10, 2002


SEAN MCGARRY
PRIMARY EXAMINER
1635